

## PHARMACOLOGICAL ACTIONS OF *APIUM GRAVEOLENS*: A REVIEW

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### Summary

The medicinal plants are widely used by the traditional medical practitioners for curing various diseases. In traditional systems of medicine, the different parts (leaves, stem, flower, root, seeds and even whole plant) of *Apium graveolens* (known as *celery* in english) are used for certain diseases. It is a small herb seen throughout India, have been recommended for the treatment of liver and spleen diseases, bronchial asthma, malaria, diarrhea, dysentery, skin diseases, arthritis, painful eye diseases, chronic fever, insect bite. The *Apium graveolens* has also been suggested to possess anti-inflammatory activity, antimicrobial, hepatoprotective, antiemetic, antispasmodic, analgesic and diaphoretic actions.

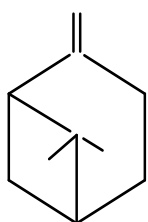
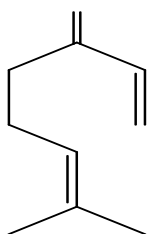
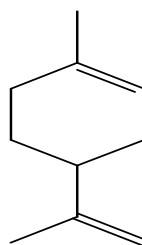
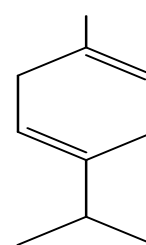
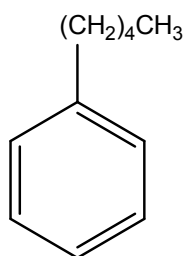
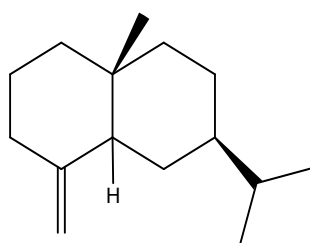
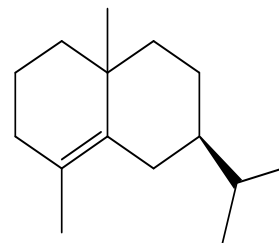
**Keyword:** Apium graveolens ,umbelliferae, pharmacological activity

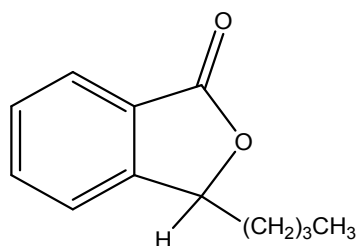
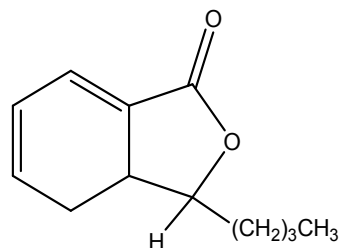
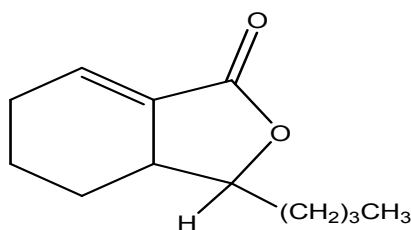
### Introduction

*Apium graveolens* is of family umbelliferae (apiaceae), grows wild at the base of the north western Himalayas and outlying hills in Punjab and in western india. The fruit, popularly known as celery seeds. A number of plants have been shown to lower serum the cholesterol level in human and experimental animals. Aqueous celery extract for 8 weeks treatment causes a significant reduction of serum total cholesterol (TC) level in growing genetically hypercholesterolaemic (RICO) rats. Daniel Tsi, Benny KH Tan was reported the mechanism underlying the hypocholesterolaemic activity of aqueous celery extract, is of its butanol and aqueous fractions ingenetically hypercholesterolaemic rico rats(1). Polyherbal formulation is reported to have hepatoprotective activity which are available in the india market. Anubha singh, S.S. Handa also reported hepatoprotective activity of apium graveolens against paracetamol and thioacetamid intoxication in rats(2). Plant *Apium graveolens*, is grown in Iraq and was assessed for its anti-inflammatory activity in rats by measuring the suppression of carrageenan-induced paw edema (3).The traditional seeds of apium graveolens used in India to treat bronchitis, asthma, liver and spleen diseases.The results also shown that, celery leaf extracts of suspension produce anti pyretic effect (4).

**Botanical and chemical constitutions**

The apium graveolens has been cultivated for the last 3000 years, notably in pharaonic Egypt, and was known in China in the fifth century BC. Apium graveolens has been used as a food at many times and the whole plant and the seeds have also been consumed as a medicine. The characteristic odors of apium graveolens are due to the presence of essential oil and phthalide derivatives. The Sedanolide, sedanonic anhydride, 3-*n*-butyl phthalide and other minor phthalides are reported to be the major constituents of apium graveolens seed oil (5). Seed of apium graveolens is extracts are used as flavoring agents for preparing herbal combinations in the pharmaceutical industries. The fruit constitutes essential oil (2-3%) Limonene (main 60%),  $\beta$ -pinene,  $\beta$ -myrcene, sedanolide pentylbenzene  $\gamma$ -terpenen selinene (10%), furocoumarins, gucoside of furocoumarin and flavonoids (6). The furanocoumarins (psoralens) phytoalexins are believed to be associated with apium graveolens is resistance to pathogen during storage (7). The investigation of the European cultivated plants shows the presence of brassinosteroids and 2- deoxybrasiinplide in the seeds of apium graveolens. Elucidation of the naturally occurring (8). Apium graveolens has different species, *Anethum graveolens* L(9), *Lepechinia graveolens* (10), *Nauplius graveolens*(11) , *Ruta graveolens*(12) , *teloxys Graveolens*(13) , *Lippia graveolens*(14), *Senecio graveolens*(15) . Rafikali A. Momin, has reported the antifungal of compounds sedanolide and senkyunolide was isolated from the apium graveovens (16).

**CHEMICAL CONSTITUENTS OF APIUM GRAVEOLENS VOLATILE OIL (6)** **$\beta$ -PINENE** **$\beta$ -MYRCENE****LIMONENE** **$\gamma$ -TERPENENE****PENTYLBENZENE** **$\beta$ -SELINENE** **$\alpha$ -SELINENE**

**n-BUTYL PHTHALIDE****SEDANENOLIDE****SEDANOLIDE**

### Hepatoprotective properties

A. Anubha singh has reported hepatoprotective activity of the methanolic extract of the seeds of *apium graveolens*. The toxicity experienced during thioacetamide and paracetamol poisoning results from the production of a metabolite. Paracetamol is mainly metabolized in the liver to excretable glucuronide and sulphate conjugates, however hepatotoxicity of paracetamol has been attributed to the formation of toxic matabolite N-acety-p-benzoquinoneimine.

Thioacetamide S-oxide, which is a direct hapatotoxin induces centri lobular necrosis with in 3h of administration. It also been observed that thioacetamide cause specific change in the nucleolus and increased synthesis of guanine and cytosine-rich RNA and decreases ribosomal RNA the cytoplasm (Zimmerman 1976). The study indicates, the plant extracts antagonize the effect of thioacetamide by acting either as member stabilizer or by preventing the distortion of the cellular ionic environment associated with thioacetamide intoxication, or by preventing interaction of thioacetamide with the transcription process of the cells.

Hepatoprotective effect of the methanolic extract of the seed of *apium graveolens* were observed during paracetamol and thioacetamid intoxication in rats which differ in their primary mechanisms of inducing hepatotoxicity. These investigation validate in the Indian system of medicine for usage of these seeds of the plant as hepatoprotective agents. (2)

B. The methanolic extract of *apium graveolens* seeds are used significantly for anti hepatocarcinogenesis and anti proliferative activity in the liver of Wistar rats at doses (200 and 400 mg/kg b.w) (17)

Table-1: Effect of methanolic extracts of seeds of *Apium graveolens* in rats intoxicated with paracetamol

Group	SGOT (KU)	SGPT (KU)	SALP (IU)	SSDH (U/I)	SGLDH (U/l)	SBRN ( $\mu\text{mol/l}$ )	PAV%
1. Control	129.0 $\pm$ 6.4	94.4 $\pm$ 19.8	55.8 $\pm$ 11.2	4.8 $\pm$ 1.8	7.21 $\pm$ 1.60	57.4 $\pm$ 14.3	000.0
2. Paracetamol (3g/kg p.o.)	230.4 $\pm$ 22.9	213.1 $\pm$ 41.8	134.6 $\pm$ 30.1	136.6 $\pm$ 37.7	252.2 $\pm$ 82.4	159.4 $\pm$ 35.9	100.0
3. Methanolic extract of <i>A. graveolens</i> (200 mg/kg p.o.)	104.6 $\pm$ 12.8 (124.0)	77.2 $\pm$ 4.6 (114.5)	54.7 $\pm$ 24.3 (101.4)	8.0 $\pm$ 4.4 (97.6)	29.5 $\pm$ 6.5 (90.9)	33.1 $\pm$ 10.5 (123.8)	25.0

Data represent the mean  $\pm$  S.D. of 6 animals. Figures in the parenthesis indicate percent reduction in individual biochemical parameters from their elevated values caused by the hepatotoxin. a Percentage proportion of abnormal value. SGOT: Serum glutamic oxaloacetic transaminase; SGPT: Serum glutamic pyruvic transaminase

C. Bahar Ahmed has reported the methanolic extract of seeds of *apium graveolens* showed maximum anti hepatoprotective activity against CCl<sub>4</sub> induced toxicity in female rats. During the study ether extract of silymarin (10/kg) used as standard. CCl<sub>4</sub> used in dose of 1.5/kg b.w gum acacia (1%) in distillation water used as vehicle. CCl<sub>4</sub> induces fatty liver and cell necrosis and plays a significant role in inducing triacylglyceral accumulation, depletion of GSH, increased lipid per oxidation, membrane damage, and depression of protein synthesis and loss of enzymes activity. In the cytoplasmic location the damage marker enzymes GOT, GPT and LDH are released in serum. The extracts of *A. graveolens* (seeds) at dose of 250-mg/kg markedly reduced CCl<sub>4</sub> induced elevation of serum GOT, GPT, SALP and increased the level of TP and TA. It also shown the protective action against the CCl<sub>4</sub> induced liver injury by impairment of CCl<sub>4</sub>-mediated lipid per oxidation, either through decreased production of free radical derivatives or due to the antioxidant activity of the protective agent itself.

The methanolic soluble active principles like flavone and diterpene seeds of *apium graveolens* are responsible for the hepatoprotective activity. The structural integrity of the hepatocellular membrane is produced in a dose dependent manner is the evident from the protection provided as compared to the enzyme levels in CCl<sub>4</sub> treated rats. In the results author have pointed the antioxidant and hepatoprotective effects of *apium graveolens*.(18)

Table-2: Effect of various extracts of *A. graveolens* seeds on serum enzymes, alkaline phosphatase, total proteins and albumin of CCl<sub>4</sub> induced liver damage in rats

Treatment	SGPT	SGOT	SALP	TP	TA
1. Control	65.5 $\pm$ 0.0	76.66 $\pm$ 3.35	31.75 $\pm$ 1.18	7.01 $\pm$ 0.18	3.85 $\pm$ 0.27
2. CCl <sub>4</sub>	131.5 $\pm$ 1.99	169.16 $\pm$ 4.66	61.0 $\pm$ 0.99	5.58 $\pm$ 0.09	2.75 $\pm$ 0.08
3. Silymarin	64.38 $\pm$ 1.05*	169.16 $\pm$ 4.66	61.0 $\pm$ 0.99 (90.0)*	7.29 $\pm$ 0.13*	4.0 $\pm$ 0.27
5. Acetone extract	68.88 $\pm$ 5.5 (94.8)**	79.33 $\pm$ 4.66 (97.2)*	38.61 $\pm$ 1.39(76.7)*	.38 $\pm$ 0.39 (57.1)	4.57 $\pm$ 0.05 (163.6)
6. Methanol extract	64.38 $\pm$ 1.05	51.33 $\pm$ 9.33 (127.5) (101.6)*	32.69 $\pm$ 0.63 (96.9)*	8.0 $\pm$ 0.05 (171.4)* 5	28 $\pm$ 0.05(227.3)*

Values are mean±S.E.M.,  $n=5$  animals per group. Figures in the parenthesis indicate percent protection in individual biochemical parameters from their elevated values caused by the hepatotoxin. The % of protection is calculated as  $100 \times (\text{values of CCl}_4 \text{ control} - \text{values of sample}) / (\text{values of CCl}_4 \text{ control} - \text{values of control})$ . SGOT: Serum glutamic oxaloacetic transaminase; SGPT: Serum glutamic pyruvic transaminase

### Hypocholesterolaemic properties

Daniel Tsi, has reported, the experimental studies of aqueous celery extract for 8 weeks treatment causes a significant reduction in serum total cholesterol (TC) level in growing genetically hypercholesterolaemic (RICO) rats. In addition, administration of butanol fraction (Fbu) and aqueous fraction (Faq) of celery extract by intra peritoneal (i.p.) infusion effectively decreases the serum TC and high-density lipoprotein cholesterol (HDL-C).

The data indicated in the table-3 shows increased excretion of  $^{14}\text{C}$ -cholesterol or its metabolites in the treated RICO rats. The radioactivity was detected with treated apium graveolens group was about twice to that of the control group.

Table-3: Serum TC concentrations and various lipoprotein cholesterol concentrations in RICO rats

Serum lipid parameters (mg/100 ml)	Control Group (n=4)	Fbu-treated Group (n=4)	Faq-treated Group (n=5)
TG	157.1 + 11.9	145.5+12.9	143.9 + 12.6
VLDL-C	28.5 f 2.8	26.1 f 1.2	22.4 f 2.1
LDL-C	52.5 f 1.5	49.7 f 3.6	46.7 f 4.8
HDL <sub>c</sub>	19.4 f 1.0	7.2 + 3.6*	3.2 f 0.9*
HDL <sub>r</sub> -C	61.8 + 1.6	48.7 f 2.3*	50.5 f 3.3*
HDL-C	81.1 k 2.5	55.9 + 5.9*	53.8 f 3.9*

The hypocholesterolaemic activity study in 8 weeks treatments of drinking aqueous exact of apium graveolens and 7-day i.p. infusion of Fbu and Faq in RICO rats was observed. HMG-CoA reductase activity of RICO rats was not affected by treatment with Fbu and Faq. The hypocholesterolaemic mechanism of plant indicated, the effective increased in the excretion of bile acid in the faeces seems to be the primary mechanism responsible for the hypocholesterolaemic effect of both the Fbu and Faq. The bile acid excretion represents the major pathway for cholesterol degradation/removal from the body. In the liver, conversion of cholesterol to bile acids is regulated by the rate limiting enzyme, cholesterol 7 $\alpha$ -hydroxylase. This implies that apium graveolens might be promoting the catabolism of cholesterol to bile acids in the liver by the enzymes cholesterol 7 $\alpha$ -hydroxylase. The study also indicated the presence of polar compounds with sugar or amino acid side chains could contribute the hypocholesterolaemic effect of extracts of apium graveolens (1).

### Anti-inflammatory properties

A. Muhaned k. al-hindawi, and Lewis has reported anti inflammatory activity of plant in the experimental studies of edema induced in rat hind paw by the local injection of carrageen and is mediated like many other edema processes also by the initial release of histamine and 5-hydroxytryptamine causing increased vascular permeability. The uses of the plant materials in the treatment of the various inflammatory reactions, particularly rheumatism is a common practice both in modern and folk medicine. Apium graveolens plant has been specifically recommended for the treatment of rheumatism. The plant extracts of apium graveolens produce dose dependent suppression of carrageen induce rat paw edema (3).

- B. Lewis, reported apium graveolens containing phytosterol is responsible for anti-inflammatory activity but it was concluded that the major anti-inflammatory effect was due to unidentified polar substances. Mannitol has been reported to reduce inflammation in adjuvant-induced arthritis in the rat. It was concluded that stem of apium graveolens also possess anti-inflammatory properties and used as a medicinal treatment for rheumatic disease (19).
- C. Falcarinol and falcarindiol are the active constituent present in the apium graveolens have shown anti-inflammatory and anti-platelet-aggregatory effects. The falcarinol have an ability to inhibit lipoxygenases and to modulate prostaglandin catabolism by inhibiting the prostaglandin-catabolizing enzyme 15-hydroxy-prostaglandin dehydrogenase (20).

Table-4: Acute ld/50 values, treatment dose and percentage inhibition of Carrageenan-induced edema in the rat paw after the intraperitoneal Injection of acetylsalicylic acid and the plant extract under study

Treatment,	LD <sub>50</sub> ,i.p(mg/kg)	treatment dose, i.p		N	+3hPaw volume (ml)	Inhibition (%)
		Exact(mg/kg)	Fresh plant equivalent(g/kg)			
1.Control(carrageenan)	-	-	-	35	0.389±0.025	-
2.Acetylsalicylic acid	500*	100.0	-	29	0.263±0.028**	32.4
3.Apium graveolens	3587	3587.7	3.40	10	0.183±0.037**	53.0

- D. A.H. Atta, A. Alkofahi, has reported anti-inflammatory effects of apium graveolens in two animal models xylene-induced ear swelling in mice model and the cotton pellet granuloma in rats. They were selected to represent acute (exudative phase) and chronic (the poliferative phase) inflammation models respectively. The present results demonstrate that ethanolic extracts of apium graveolens (dose dependent) of 200 or 400mg/kg p.o produce anti-inflammatory effects due to presence of volatile oils, flavenoids and resins. The traditional indication of these plant extracts are used for inflammation and pain associated with sprains, bruises, wounds, spasmodic colics and rheumatic arthritis (21).

Table-5: Effect of ethanolic extracts on xylene-induced ear swelling in mice

Ethanolic Extract	200 mg/kg Weight (mg )	Inhibition (%)	400 mg/kg Weight (mg)	Inhibition (%)
1.Normal saline	4.3±1.9	49	3.4±1.4	-
2.apium graveolens	3.6±0.9	16	3.2±1.0	12

A dose of 100 and 200 mg/kg b. wt.  $P \leq 0.05$ ,  $P \leq 0.01$ . Mean  $\pm$  S.D.  $n=5$

### Side Effect, Toxicity And Contraindications

F.R.Widmann, have reported the furano coumarin and psoralin found in aqueous exact of apium graveolens causes mice to develop carcinomas when exposed to long wavelength ultraviolet light(1). Apium graveolens is well recognized for its importance as an allergen in Central Europe it triggers severe allergic reactions, which are mandatory for labeling on food products within the European Union since 2005.

Also in aged apium graveolens allergic patients (mean age 72 years) properly digested apium graveolens showed decreased capacity to bind and cross link IgE as evaluated by skin tests and IgE immune blot. Thus, in the geriatric murine model, apium graveolens allergy was induced only if gastric digestion was hindered. Accordingly, gastric proteolysis decreased in vitro and in vivo IgE-reactivity against apium graveolens proteins in aged allergic patients,(22).In Switzerland, it ranks among the most prevalent food allergies and has been reported as the most frequent cause of food anaphylaxis. Approximately 50% of apium graveolens produce allergic reaction was observed in the Switzerland and presented a case history of systemic allergic reactions (23).

### **Conclusion**

The above observations shown that the methanolic extracts of the seeds of *A. graveolens* and aerial part of the plant leaf, stem, showed maximum antihepatotoxic activity, Anti-inflammatory activity, hypocholesterolaemic activity in rats. The activity of the tested samples was compared to that of standards and controls where mention in the above observation. The isolated constituents of methanolic soluble active principles like flavone and diterpene and polar substances mannitol furanocoumarin and psoralin likely to be responsible for the pharmacological activity of the plant *Apium graveolens*.

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